

US Patent Application No. 10/663,506  
Response to OA mail date 5/4/2006

AM-101106US

### AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

#### **Listing of Claims:**

1. (Currently Amended) A pharmaceutical composition for oral administration comprising a granulation, said granulation comprising rapamycin 42-ester with 3-hydroxy-2-(hydroxymethyl)-2-methylpropionic acid CCI-779, a water soluble polymer, a surfactant, an antioxidant from 0.001% to 3% (wt/wt), and a pH modifying agent.
2. (Original) The composition of claim 1, wherein the water soluble polymer is PVP, hydroxypropylmethylcellulose, polyethylene glycol, or cyclodextrin or mixtures thereof.
3. (Original) The composition of claim 2, wherein the water soluble polymer is PVP.
4. (Original) The composition of claim 3, wherein the surfactant is polysorbate 80, sodium lauryl sulfate, sodium dodecyl sulfate, a salt of a bile acid, an ethoxylated vegetable oil, a polyoxyethylene-polyoxypropylene block copolymer, or a poloxamer.
5. (Original) The composition of claim 4, wherein the surfactant is sodium lauryl sulfate or sodium dodecyl sulfate.
6. (Original) The pharmaceutical composition of claim 5, wherein the pH modifying agent is sodium citrate, citric acid, or dilute hydrochloric acid.
7. (Withdrawn-Currently Amended) A process for preparing a rapamycin 42-ester with 3-hydroxy-2-(hydroxymethyl)-2-methylpropionic acid CCI-779-oral composition, which comprises:

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- (a) dissolving rapamycin 42-ester with 3-hydroxy-2-(hydroxymethyl)-2-methylpropionic acidCCI-779 and from 0.001% to 3% (wt/wt) of an antioxidant in an alcohol to form an alcoholic solution;
- (b) dissolving PVP, a pH modifying agent, and a surfactant in water to form an aqueous solution;
- (c) mixing the alcoholic solution and the aqueous solution to form a hydrocoholic solution.
- (d) adding the hydrocoholic solution to a mixer containing one or more intragranular excipients;
- (e) granulating the mixture; and
- (f) drying the resulting granulation.

8. (Withdrawn-Currently Amended) A process for preparing a rapamycin 42-ester with 3-hydroxy-2-(hydroxymethyl)-2-methylpropionic acidCCI-779 oral composition, which comprises:

- (a) dissolving rapamycin 42-ester with 3-hydroxy-2-(hydroxymethyl)-2-methylpropionic acidCCI-779 and from 0.001% to 3% (wt/wt) of an antioxidant in an alcohol to form an alcoholic solution;
- (b) dissolving PVP, a pH modifying agent, and a surfactant in water to form an aqueous solution;
- (c) adding the aqueous and alcoholic solutions stepwise, and in one or more portions each, to a mixer containing one or more intragranular excipients;
- (ed) granulating the mixture; and
- (fe) drying the resulting granulation.

9. (Cancelled)

10. (Currently Amended) A rapamycin 42-ester with 3-hydroxy-2-(hydroxymethyl)-2-methylpropionic acidCCI-779 oral composition prepared by the process comprising;

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- (a) dissolving rapamycin 42-ester with 3-hydroxy-2-(hydroxymethyl)-2-methylpropionic acidCCI-779 and from 0.001% to 3% (wt/wt) of an antioxidant in an alcohol;
- (b) dissolving PVP, a pH modifying agent, and a surfactant in water;
- (c) combining the aqueous and alcoholic solutions to provide a hydroalcoholic solution;
- (d) adding the hydroalcoholic solution to a mixer containing one or more intragranular excipients;
- (e) granulating the mixture; and
- (f) drying the resulting granulation.

11. (Original) The composition of claim 10, wherein the pH modifying agent is selected from the group consisting of citric acid, sodium citrate, hydrochloric acid and mixtures thereof.

12. (Original) The composition of claim 11, wherein the alcohol is ethanol.

13. (Original) The composition of claim 12, wherein the antioxidant is butylated hydroxyanisole and butylated hydroxytoluene.

14. (Original) The composition of claim 13, wherein the surfactant is sodium lauryl sulfate.

15. (Currently Amended) A rapamycin 42-ester with 3-hydroxy-2-(hydroxymethyl)-2-methylpropionic acidCCI-779 oral formulation prepared by the process comprising:

- (a) dissolving rapamycin 42-ester with 3-hydroxy-2-(hydroxymethyl)-2-methylpropionic acidCCI-779 and from 0.001% to 3% (wt/wt) of an antioxidant in an alcohol;
- (b) dissolving PVP, a pH modifying agent, and a surfactant in water;

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- (c) adding the aqueous and alcoholic solutions stepwise, and in one or more portions each, to a mixer containing one or more intragranular excipients;
- (ed) granulating the mixture; and
- (fe) drying the resulting granulation.

16. (Original) The composition of claim 15, wherein the pH modifying agent is selected from the group consisting of citric acid, sodium citrate, hydrochloric acid and mixtures thereof.

17. (Original) The composition of claim 16, wherein the alcohol is ethanol.

18. (Original) The composition of claim 17, wherein the antioxidant is butylated hydroxyanisole and butylated hydroxytoluene.

19. (Original) The composition of claim 18, wherein the surfactant is sodium lauryl sulfate.